following paragraph:

A1

(Fig 1C) DNA sequence of the SML1 region (SEQ ID NO: 1) is shown with the predicted amino acid sequence of the SML1 ORF (SEQ ID NO: 2). Two 11 base pair direct repeats are underlined. The putative TATA box is indicated by large bold letters.

On page 10, lines 29-35, please delete the paragraph which begins "The present invention provides . . ." and insert the following paragraph:

A2

The present invention provides for an isolated Sml1 protein or a homologue thereof. In one embodiment, the Sml1 protein has the amino acid sequence shown in Figure 1C. In another embodiment, the Sml1 protein is a homologue, such as a human Sml1 protein, a rat Sml1 protein, a mouse Sml1 protein, a microbial Sml1 protein, a plant Sml1 protein, or an insect Sml1 protein.

On page 44, lines 18-22, please delete the paragraph which begins "To follow the sml1-1 allele. . ." and insert the following paragraph:

A3

To follow the sml1-1 allele in genetic crosses, yeast colony PCR reactions were carried out (Adams et al., 1997). Using primer pair A (SEQ ID NO:3) and C (SEQ ID NO: 4) (Table 4), the wild-type and the sml1-1 alleles give rise to 570 bp and 280 bp PCR products, respectively.

On page 44, lines 24-37, please delete the paragraph which begins "To test whether overproduction. . ." and insert the following paragraph:

A4

To test whether overproduction of Mec1 rescues rad53

lethality, a GAL-MEC1 plasmid (pWJ701) was constructed. The native promoter of MEC1 on pRS416-MEC1 was replaced with a GAL1-10 promoter fragment (generated from a PCR reaction using primer pair p416-GAL 5' (SEQ ID NO: 9) and MEC1-GAL 3' (SEQ ID NO: 10), Table 4) through in vivo DNA recombination (Ma et al., 1987). This plasmid was then transformed into rad53Δ/RAD53 sml1-1/SML1 heterozygous diploids. After dissection of 66 total tetrads from six different transformants, no rad53Δ {pGAL-MEC1} spores were recovered on galactose-inducing medium. However, in the same dissections, the pRS416-MEC1 plasmid segregated into RAD53 or rad53 sml1 spores normally. Moreover, in a separate experiment, rad53Δ strains cannot lose a CEN-RAD53 plasmid (pWJ676) even when MEC1 is overexpressed.

A4

On page 45, lines 8-19, please delete the paragraph which begins "Gene disruptions for . . ." and insert the following paragraph:

Gene disruptions for SML1 and DUN1 were performed as described by Baudin et al. (1993). Forty-five base pairs of homology adjacent to each ORF was added to HIS3 and URA3 selectable markers, respectively, by PCR with the primers listed in Table 4 (SML1-HIS3 5' (SEQ ID NO: 5) & SML1-HIS3 3' (SEQ ID NO: 6) and dun1d 5' (SEQ ID NO: 7) & dun1d 3' (SEQ ID NO: 8)). MEC1 was disrupted in diploids using a fragment that contains the 800 bp TRP1 marker (from pUC18-TRP1) replacing the sequence from 98 bp to 7764 bp (BamHI-SacII) of the MEC1 ORF (Rothstein, 1983). RAD53 was disrupted by transforming the EcoRI fragment containing rad53Δ::HIS3 (Zheng et al., 1993). All disruptions were confirmed by genomic blots and genetic analysis.

A5

On page 47, lines 20-34, please delete the paragraph which begins "The strains and plasmids for . . ." and insert the following paragraph:

The strains and plasmids for two-hybrid analysis were PJ69-4A, pGBD-C2, pGAD-C2 (James et al., 1996) and pACTII (CLONTECH® Inc.). The primer pair pB-SML1 5' (SEQ ID NO: 11) and pGBD-SML1 3' (SEQ ID NO: 13) (Table 4) was used to amplify the SML1 ORF. After digestion with BamHI and PstI, this PCR product was cloned into the BamHI-PstI sites of pGBD-C2 to construct plasmid pWJ728. Similarly, plasmid pWJ684 contains a BamHI fragment from the PCR product of the SML1 ORF generated using the primer pair pB-SML1 5' and pB-SML1 3' (SEQ ID NO: 12) (Table 4) and inserted at the BamHI site of pACTII. PCR fragments containing the RNR1 or the RNR2 ORF were generated by primer pairs RNR1-ORF 5' (SEQ ID NO: 14) and RNR1 3' (SEQ ID NO: 15) or RNR2-ORF 5' (SEQ ID NO: 17) and RNR2 3' (SEQ ID NO: 16) (Table 4). These fragments were cloned into the BamHI-PstI site of pGBD-C2 and pGAD-C2 to construct pWJ731 and pWJ745 or pWJ729 and pWJ746 respectively.

A6

On page 48, lines 6-16, please delete the paragraph which begins "The GST-Rnr1 fusion plasmid,. . ." and insert the following paragraph:

The GST-Rnr1 fusion plasmid, pWJ744, was generated by inserting a BamHI-SalI fragment from the PCR product of the RNR1 ORF generated using primers RNR1-5'+0 (SEQ ID NO: 18) and RNR1 3' far (SEQ ID NO: 19) into the BamHI-SalI sites of pEG(KT) (Mitchell et al., 1993). The SML1 ORF was amplified using primer pYX-SML1 5' (SEQ ID NO: 20) and pB-SML1 3' and the BamHI-digested PCR product was cloned into BamHI site of pYX423. Next, an EcoRI fragment of a 3XHA tag (Schneider et al., 1995) generated after PCR using primer pair HA 5' (SEQ ID NO: 21) and HA 3' (SEQ ID NO: 22) was added to the N-terminus of SML1 to construct plasmid pWJ699. Both pWJ744 and pWJ699 can functionally complement rnr1 and

A7

A7

sml1, respectively.

On page 51, lines 23-38, please delete the paragraph which begins "**Recombinant proteins and peptides.**" and insert the following paragraph:

Recombinant proteins and peptides. The recombinant yeast proteins Rnr1, Rnr2 and Rnr4 were expressed in E. coli BL21(DE3) bacteria using the pET3a expression vector; mouse recombinant proteins R1 and R2 were expressed in E. coli BL21(DE3)pLysS bacteria using the same vector (14). Purification of the recombinant mouse and yeast R1 proteins, and of the recombinant mouse R2 protein, was made as described earlier (15,16). The yeast Rnr2 and Rnr4 proteins were coexpressed and purified as a heterodimer[3]. The SML1 coding sequence (13) was amplified by PCR from yeast genomic DNA using the following oligonucleotides: 5'-CAA TAA TTT CCC CAT ATG CAA AAT TCC-3' (SEQ ID NO: 23) and 5'-AAA GGA TCC TTA GAA GTC CAT TTC CTC GAC-3' (SEQ ID NO: 24). After the PCR product was cleaved with NdeI and BamHI restriction endonucleases, it was cloned into the pET3a vector digested with the same restriction enzymes. The SML1 sequence in the resulting plasmid was checked by DNA

A8

On page 52, lines 15-17, please delete the paragraph which begins "N-acetylated peptides corresponding to . . ." and insert the following paragraph:

A9

N-acetylated peptides corresponding to the last 9 amino acids of either Rnr2p (GAFTFNEDF) (SEQ ID NO: 25), Rnr4p (KEINFDDDF) (SEQ ID NO: 26) or Sml1p (QGKVEEMDF) (SEQ ID NO: 27) were ordered from Genosys.